Hodgkin’s Lymphoma

DIAGNOSIS

- FNA alone is insufficient
- Hematopathology review of all slides with at least one tumor paraffin block. Rebiopsy if consult material is non-diagnostic
- Core needle biopsy may be adequate if diagnostic, but an excisional nodal biopsy is recommended
- Recommend staining for CD15, CD30, T and B panels, CD20, PAX5
- Adequate immunophenotype to confirm diagnosis
  - Paraffin panel for Hodgkin’s lymphoma (HL) including nodular lymphocyte predominant HL:
    - CD20, PAX-5, CD30, CD3, CD15, and CD45 (LCA)
    - EBER
- EBV proteins (i.e., LMP1) recommended for nodular sclerosis (NS) grade 2 or anaplastic variants

OF USE IN CERTAIN CIRCUMSTANCES

- Immunohistochemical studies:
  - LMP1
  - BOB1, OCT2, and CD79a (differential diagnosis with B-cell lymphoma, unclassifiable with features intermediate between classical HL and DLBCL and primary mediastinal large B-cell lymphoma).
  - CD21, CD23, or CD35 (follicular dendritic cell markers), CD57, BCL6 and IgD in cases of nodular lymphocyte predominant HL. (may help with T-cell/histiocyte rich large B-cell lymphoma)
  - CD2, CD43, ALK, and EMA (differential diagnosis with anaplastic large cell lymphoma)

STRONGLY RECOMMEND:

- Core biopsy for tissue banking by protocol

WORKUP

- History and physical including:
  - Alcohol intolerance
  - Pruritus
  - Exam of nodes
  - B symptoms (fever, sweats, weight loss)
  - CBC, differential, platelets
  - LDH, liver function tests (LFTs) including: alkaline phosphatase, AST, ALT, and albumin, BUN, creatinine
  - Erythrocyte sedimentation rate (ESR)
  - Screening for HIV 1, HIV 2, hepatitis B and C (HBcAb, HBsAg, HCVAb)
  - Chest x-ray
  - CT neck, chest, abdomen and pelvis
  - PET/CT
  - Bilateral bone marrow biopsies
  - Multigated acquisition (MUGA) scan or echocardiogram
  - Counseling: fertility, psychosocial if clinically indicated
  - Lifestyle risk assessment

USEFUL IN SELECTED CASES:

- Pregnancy test: women of childbearing potential
- Discuss fertility issues and sperm banking for patients of childbearing potential
- Semen cryopreservation, if chemotherapy or pelvic radiotherapy contemplated
- Cardiology consultation at baseline if risk factors for cardiac toxicity [i.e., obesity, abnormal echocardiogram, hypertension (HTN), hyperlipidemia (HLD)]

See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

NOTE: Consider Clinical Trials as treatment options for eligible patients.
Hodgkin’s Lymphoma

CLINICAL PRESENTATION

Classical Hodgkin’s Lymphoma
Stage I-II, without bulky disease

Classical Hodgkin’s Lymphoma
Stage I-IIB, bulky disease

Favorable\(^1\) without any evidence of the following:
- Elevated ESR greater than or equal to 50 mm/hour for stages I and IIA
- Elevated ESR greater than or equal to 30 mm/hour for stages IB and IIB
- Nodal regions greater than or equal to 3\(^1\)
- Extranodal disease\(^2\)

Unfavorable\(^3\) with any evidence of the following:
- Elevated ESR greater than or equal to 50 mm/hour for stages I and IIA
- Elevated ESR greater than or equal to 30 mm/hour for stages IB and IIB
- Nodal regions greater than or equal to 3\(^1\)
- Extranodal disease\(^2\)

PRIMARY TREATMENT

ABVD for 2 cycles and 20 Gy of involved site radiation therapy\(^4\)

See Page 4 for response assessment

- ABVD for 6 cycles and 30 Gy of involved site radiation therapy\(^4\)
  or
- Consider ABVD for 4 cycles and 30 Gy of involved site radiation therapy\(^4\)

ABVD = doxorubicin, bleomycin, vinblastine, dacarbazine

\(^1\) See Diagram 1 on page 7 for German Hodgkin’s Study Group (GHSG) Schematic of Nodal Sites
\(^2\) Extranodal disease (i.e., any tumor spread that involves tissues other than those of the lymph nodes, spleen, thymus, Waldeyer’s tonsillar ring, appendix, and Peyer’s patches)
\(^3\) See Appendix A for Unfavorable Factors – risk as defined by Hasenclever’s Model
\(^4\) See Appendix B for Radiation Therapy Guideline

NOTE: Consider Clinical Trials as treatment options for eligible patients.

Abramson, M. S., & Pahor, M. (2019). Lyon’s Textbook of Medicine (20th ed.). Elsevier. This practice algorithm has been specifically developed for MD Anderson using a multidisciplinary approach and taking into consideration circumstances particular to MD Anderson, including the following: MD Anderson’s specific patient population; MD Anderson’s services and structure; and MD Anderson’s clinical information. Moreover, this algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers. This algorithm should not be used to treat pregnant women.
CLINICAL PRESENTATION

Classic Hodgkin’s Disease
Advance Stages III, IV

Lymphocyte Predominant Hodgkin’s Disease Stages I, II

Lymphocyte Predominant Hodgkin’s Disease Stages III, IV

PRIMARY TREATMENT

ABVD for 6 cycles with or without 30 Gy of involved site radiation therapy

• Involved site radiation therapy
• Consider R-CHOP times 4 followed by involved site radiation for patients with bulky disease

R-CHOP for 3-6 cycles

See Page 4 for Response Assessment

ABVD = doxorubicin, bleomycin, vinblastine, dacarbazine
R-CHOP = rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone

1 Advanced stage is consistent with an International Prognostic Score (IPS); Consider BEACOPP chemotherapy regimens for Advanced Stage Clinical Hodgkin’s lymphoma
2 See Appendix B for Radiation Therapy Guideline
3 R-CHOP for 3-4 cycles followed by involved site radiation therapy also an option

NOTE: Consider Clinical Trials as treatment options for eligible patients.
NOTE: Consider Clinical Trials as treatment options for eligible patients.

End of Therapy Response Assessment and Treatment of Classical Hodgkin's and Lymphocyte Predominant Hodgkin's

- **PET Deauville\(^1\) 1-3**
  - Consider involved site radiation therapy if part of original treatment plan

- **PET/CT of previously positive areas**

- **PET Deauville\(^1\) 4**
  - Consider biopsy\(^2\) or
  - Repeat PET or
  - Proceed to radiation therapy

- **PET Deauville\(^1\) 5**
  - Consider partial remission or less
  - Consider biopsy\(^2\) and salvage

- **See Follow-up After Completion of Treatment on Page 5**

See Appendix C for Deauville Criteria

If biopsy positive, consider salvage treatment
If biopsy negative, observation or consider radiation

See Appendix E for Chemotherapy Regimens
FOLLOW-UP AFTER COMPLETION OF TREATMENT

- Follow-up with an oncologist is recommended
- Interim history and physical: every 4 months for years 1 and 2, then every 6 months for years 3-5, then annually
- Pneumococcal and meningococcal revaccination every 6 years, if patient treated with splenic radiotherapy
- Annual influenza vaccine (especially if patient treated with bleomycin or chest radiotherapy)
- Laboratory studies:
  - CBC, platelets, chemistry profile (LDH, LFTs including: alkaline phosphatase, AST, ALT, albumin, BUN and creatinine)
    - every 4 months for years 1 and 2, then every 6 months for years 3-5, then annually
  - TSH every 6 months if radiotherapy to neck and optional for all other cases
- CT chest/abdomen/pelvis 1 to 2 times during first year, then exam, chest x-ray, and labs for monitoring
- Annual breast screening: initiate alternating mammography and MRI 8 years post therapy or at age 35, whichever is sooner, if radiotherapy above diaphragm
- Counseling: reproduction, health habits, psychosocial, cardiovascular, breast self-exam, skin cancer risk, end-of-treatment discussion
- Recommend written follow-up instructions for the patient
- Stress test/echocardiogram at 10 year intervals after treatment is completed
Hodgkin’s Lymphoma

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NOTE: Consider Clinical Trials as treatment options for eligible patients.

**PATIENT PRESENTATION**

Post-first-line therapy, chemotherapy with no radiation therapy or first-line therapy combination of chemotherapy with radiation therapy

Relapse or Refractory disease

**SALVAGE THERAPY**

Consider:
- ICE
- DHAP
- IGEV
- GND

Complete response¹ (CR)

- AHSCT²,³ with or without locoregional radiation therapy
- Consider maintenance brentuximab vedotin for patients with primary refractory disease, early relapse less than 12 months or extranodal disease⁴ at time of relapse if patients are not in CR at time of AHSCT or if brentuximab vedotin was given as a salvage treatment and induced remission

Progressive disease post AHSCT?

- Yes
  - Brentuximab vedotin
  - Clinical trial

- No
  - Monitor as clinically indicated (see Page 5)

Partial response¹ (PR)

Consider change to a different regimen including brentuximab vedotin

Complete response or near complete response?

- Yes
  - Consider novel therapies on clinical protocols or gemcitabine-based chemotherapy regimens if not previously given

- No

AHSC = autologous hematopoietic stem cell transplant
DHAP = high dose cytarabine, cisplatin, and dexamethasone
GND = gemcitabine, navelbine, and doxorubicin liposomal
ICE = ifosfamide, carboplatin, and etoposide
IGEV = ifosfamide, gemcitabine, vinorelbine, and prednisone

¹ See Appendix D for Response Criteria for Malignant Lymphoma
² Biopsy if plan to treat with high-dose chemotherapy
³ Conventional-dose chemotherapy may precede high-dose therapy. Sequence of therapy may vary
⁴ Extranodal disease (i.e., any tumor spread that involves tissues other than those of the lymph nodes, spleen, thymus, Waldeyer’s tonsillar ring, appendix, and Peyer’s patches)
⁵ Selection of chemotherapy should be individualized

Department of Clinical Effectiveness V5
Approved by the Executive Committee of the Medical Staff on 02/27/2018

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APPENDIX A: Unfavorable Factors

**Localized Presentations**
- Bulky mediastinal mass
- Elevated ESR greater than or equal to 50 mm/hour for stages I and IIA
- Elevated ESR greater than or equal to 30 mm/hour for stages IB and IIB
- Nodal regions greater than or equal to 3
- Extranodal disease

**Advanced Disease (International Prognostic Score)**
- Albumin less than 4 g/dL
- Hemoglobin less than 10.5 g/dL
- Male
- Age greater than or equal to 45 years
- Stage IV disease
- Leukocytosis (white blood cell count at least 15 K/microliter)
- Lymphocytopenia (lymphocyte count less than 8% of white blood cell count, and/or lymphocyte count less than 0.6 K/microliter)

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1 Extranodal disease (i.e., any tumor spread that involves other tissues than those of the lymph nodes, spleen, thymus, Waldeyer’s tonsillar ring, appendix and Peyer’s patches)
Hodgkin’s Lymphoma

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APPENDIX B: Radiation Therapy Guidelines

Radiation Therapy Guidelines

Doses if radiation therapy is given alone:
- 30 Gy: Involved site
  - With consideration of IMRT or proton therapy, as appropriate, to minimize toxicity
- Bulky lesions, greater than 5 cm: consider 36 Gy to involved site

Doses for combined modality radiation therapy:
- Stage I-II, non bulky disease, favorable: 20 Gy to involved site
- Stage I-II, non bulky disease, unfavorable: 30 Gy to involved site
- Stage I-II, bulky, regardless of other risk factors: 30 Gy to involved site

Salvage Radiation Therapy Guidelines when Deauville greater than or equal to 4:
- Involved site radiation dose of 40-50 Gy

RADIATION FIELDS

Involved site: involved lymphoid region(s) only

APPENDIX C: Deauville Criteria

- Score 1: no uptake
- Score 2: uptake less than or equal to mediastinum
- Score 3: uptake greater than mediastinum but less than or equal to liver
- Score 4: uptake greater than liver at any site
- Score 5: uptake greater than liver and new sites of disease
- Score X: new areas of uptake unlikely to be related to lymphoma

A score of 1-3 is regarded as negative and 4 or 5 as positive
## APPENDIX D: Response Criteria for Malignant Lymphoma

<table>
<thead>
<tr>
<th>Response Category</th>
<th>Nodal Masses</th>
<th>Spleen, Liver</th>
<th>Bone Marrow</th>
</tr>
</thead>
</table>
| CR (Complete Response: disappearance of all evidence of disease) | • FDG-avid or PET positive prior to therapy; mass of any size permitted if PET negative  
• Variously FDG-avid or PET negative; regression to normal size on CT | Not palpable, nodules disappeared                                            | Infiltrate cleared on repeat biopsy; if indeterminate by morphology, immunohistochemistry should be negative |
| PR (Partial Response)      | • Greater than or equal to 50% decrease in SPD of up to 6 largest dominant masses; no increase in size of other nodes  
• FDG-avid or PET positive prior to therapy; one or more PET positive at previously involved site  
• Variously FDG-avid or PET negative; regression on CT | Greater than or equal to 50% decrease in SPD of nodules (for single nodule in greatest transverse diameter); no increase in size of liver or spleen | Irrelevant if positive prior to therapy; cell type should be specified |
| SD (Stable disease: failure to attain CR/PR or PD) | • FDG-avid or PET positive prior to therapy; PET positive at prior sites of disease and no new sites on CT or PET  
• Variously FDG-avid or PET negative; no change in size of previous lesions on CT | Greater than 50% increase from nadir in the SPD of any previous lesions | New or recurrent involvement |
| Relapse or Progressive disease (Any new lesion or increase by greater than or equal to 50% of previously involved sites from nadir) | • Appearance of a new lesion(s) greater than 1.5 cm in any axis, greater than or equal to 50% increase in SPD of more than one node, or greater than or equal to 50% increase in longest diameter of a previously identified node greater than 1 cm in short axis  
• Lesions PET positive if FDG-avid lymphoma or PET positive prior to therapy | Greater than 50% increase from nadir in the SPD of any previous lesions | New or recurrent involvement |

FDG, $[^{18}F] = $ fluorodeoxyglucose  
SPD = sum of the product of the diameters

# Hodgkin’s Lymphoma

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## APPENDIX E: Chemotherapy Regimens for Hodgkin’s Disease

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Contents</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABVD</td>
<td>doxorubicin, bleomycin, vinblastine, and dacarbazine</td>
</tr>
<tr>
<td>ASHAP</td>
<td>doxorubicin, methylprednisolone, high dose cytarabine, cisplatin</td>
</tr>
<tr>
<td>BEACOPP</td>
<td>bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone</td>
</tr>
<tr>
<td>CHOP</td>
<td>cyclophosphamide, doxorubicin, vincristine, prednisone</td>
</tr>
<tr>
<td>CVPP</td>
<td>cyclophosphamide, vincristine, procarbazine, prednisone</td>
</tr>
<tr>
<td>ICE</td>
<td>ifosfamide, carboplatin, and etoposide</td>
</tr>
<tr>
<td>DHAP</td>
<td>high dose cytarabine, cisplatin, and dexamethasone</td>
</tr>
<tr>
<td>IGEV</td>
<td>ifosfamide, gemcitabine, vinorelbine, and prednisone</td>
</tr>
<tr>
<td>GND</td>
<td>gemcitabine, navelbine and doxorubicin liposomal</td>
</tr>
</tbody>
</table>
SUGGESTED READINGS


Hodgkin’s Lymphoma

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SUGGESTED READINGS


Hodgkin’s Lymphoma

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DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Lymphoma Center Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

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